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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/568,691

08/30/2006

Lindsay Jane Bawden

620-418

2784

23117

7590

07/07/2010

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EXAMINER

HARRIS, ALANA M

ART UNIT

PAPER NUMBER

1643

MAIL DATE

DELIVERY MODE

07/07/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/568,691	Applicant(s) BAWDEN ET AL.	
	Examiner Alana M. Harris, Ph.D.	Art Unit 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12/07/09; 03/05/10.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,6-14,20,25-33,35 and 37-48 is/are pending in the application.
- 4a) Of the above claim(s) 37-43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,6-14,20,25-33,35 and 44-48 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>02/17/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment and Argument

1. Claims 1-3, 6-14, 20, 25-33, 35 and 37-48 are pending.

Claims 37-43, drawn to non-elected inventions are withdrawn from examination.

Claims 4, 5, 15-19, 21-24, 34 and 36 have been cancelled.

Claims 1, 7, 10, 11, 20 and 48 have been amended.

Claims 1-3, 6-14, 20, 25-33, 35 and 44-48 are examined on the merits to the extent the elected species are H4 Lys 16 (Ac) from Table 1 and H3 Lys 79 (Me) from Table 2.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objection

Claim Objections

3. The objection of claim 23 is withdrawn because the claim has been cancelled.

Withdrawn Rejections

Claim Rejections - 35 USC § 112

4. The rejection of claims 10, 11 and 48 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of the amendments to the claims. Claims 4, 5, 15-19, 21-24, 34 and 36 have been cancelled.

New Grounds of Objection

Specification

5. The attempt to incorporate subject matter into this application by reference to H3 Lys 79 (Me), SEQ ID NO: 11 is ineffective because it is not of record in the documents cited in the specification, page 4, lines 18-25 and accompanying this Action.

The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the

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material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

New Grounds and Maintained Rejections

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-3, 6-14, 20, 25-33, 35 and 44-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. ***THIS IS A NEW MATTER REJECTION.***

Applicants have supplied a Sequence Listing comprising SEQ ID NOs: 11-16. SEQ ID NO: 11 corresponds to H3 Lys 79 (Me) and SEQ ID NO: 12 corresponds to H4 Lys 16 (Ac), see claim 1 submitted December 7, 2009 and Remarks, page 18, 2nd paragraph. Applicants note these histone sequence were of public record and reference page 4 of their specification, lines 23-25, see Remarks, page 18, 2nd paragraph. The Examiner has reviewed Luger et al. (Crystal structure of the nucleosome

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core particle at 2.8 Å resolution. Nature (389): 251-260 (18 September 1997)). On page 252, Figure 1C the Examiner does note the amino acid sequence for H4 Lys 16 (Ac), SEQ ID NO: 12. Furthermore, Figure 1C caption on page 253 cites, “[s]ites of *in vivo* acetylation are indicated with a letter ‘a’, hence there is support for H4 Lys 16 (Ac). However, there seems to be no support for the methylated H3 Lys 79. Lugar does not provide support for Applicants’ methylated H3 Lys 79 (SEQ ID NO: 11). Ausio et al. (Biochem. Cell Biol. 79: 693-709, 2001) also seems to not support H3 Lys 79 (Me) and it’s corresponding sequence. Applicants should delete or specifically cite where support can be found.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. The rejection of claims 1-3, 6-14, 20, 25-33, 35 and 44-48 under 35 U.S.C. 103(a) as being unpatentable over Allis et al./ U.S. Patent Application Publication number 2006/0073517 A1 (effective filing date March 10, 2003), and further in view of Allis(b) et al./ U.S. Patent Application Publication number 2005/0069931 A1 (effective filing date

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February 19, 2003) is maintained. Claims 4, 5, 15-19, 21-24, 34 and 36 have been cancelled.

Applicants submit while the two modifications, H4 Lys 16 (Ac) from Table 1 and H3 Lys 79 (Me) from Table 2 are of record in Allis the "...document does not provided any indication that these two specific histone modifications are associated with disease", see Remarks submitted December 7, 2009, page 20. Moreover, Applicants assert Allis(b) does not teach these two specific histone modifications would be useful in the detection of disease conditions, such as cancer, see page 20 of Remarks, last paragraph. Applicants conclude arguments noting neither, Allis or Allis(b) mentions methods to detect modified histones and the possibility of detecting endogenous antibodies that bind specifically to histone modifications, see Remarks, page 22 and 23. The arguments and points of view have been carefully considered, but found unpersuasive.

Applicants are reminded that the claims do not read on antibodies that bind exclusively to H4 Lys 16 (Ac) and H3 Lys 79 (Me). The antibodies cited in the claims are not antibodies that seem to be able to distinguish between any particular modification. The antibodies of Allis are able to bind modified histones associated with a disease state. Chromatin from both normal and diseased tissues are contacted with an antibody and the staining pattern and detectable differences of the

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antibody bound chromatin isolated from normal tissue to the staining pattern of the antibody bound chromatin isolated from the diseased state is implemented in diagnosing disease, see page 19, claim 24. Allis does not teach the claimed method, wherein a biological fluid sample is obtained from an individual and the disease condition is a cancer or an autoimmune disease. Allis also does not the claimed method, wherein DNA associated with the nucleosome comprising a modified histone is isolated, amplified and sequenced.

However, Allis(b) teaches assaying isolated nucleosomes from a patient's blood or serum for specific histone amino terminus modifications as diagnostic indicators of disease, such as cancer, see abstract; page 3, section 0044; page 4, section 0059; and page 5, section 0065. Anti-modified histone antibodies are used in the assay to identify a modified histone, as well as antibodies that are capable of binding and isolating nucleosomes, see page 3, section 0049. Moreover, nucleosomes are immunoprecipitated and the associated DNA is purified, labeled and subjected to molecular analytical techniques, such as PCR and sequence analysis, see page 5, section 0061; and page 6, sections 0069 and 0070. Also taught in Allis(b) is the implementation of DNA microarrays and hybridization, see page 6, section 0068. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made based on both references to assess

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nucleosomes and modified histone proteins in a number of biological fluids and conduct protein and nucleic acid based assays in order to diagnose diseases. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings in both Allis references to assay specific histone modifications because they serve as diagnostic markers of disease, see Allis page 1, section 0010; and Allis(b) page 1, sections 0007 and 0008.

For the reasons of record and reiterated herein the rejection is maintained.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the

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mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The Examiner works a flexible schedule, however she can normally be reached Monday through Saturday, 8 am to 8 pm with alternate Fridays off.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alana M. Harris, Ph.D.
10 June 2010

/Alana M. Harris, Ph.D./

Primary Examiner, Art Unit 1643